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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/451,739	11/30/1999	DIRK JAGER	LUD-5615	9448

24972 7590 05/14/2003

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EXAMINER
NICKOL, GARY B

ART UNIT	PAPER NUMBER
1642	24

DATE MAILED: 05/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/451,739	JAGER ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *80-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80 and 85-97* is/are rejected.

7)☒ Claim(s) *81-84* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Election filed March 11, 2003 (Paper No. 23) in response to the Office Action of February 14, 2003 is acknowledged and has been entered.

Claims 1-79 were cancelled.

Claims 80-97 were added and are currently pending.

Applicant's election with traverse of Group XIII, claim 79 in Paper No 23 is acknowledged. The traversal is on the ground(s) that the subject matter of Claim 79 de facto incorporates the subject matter of Group I, drawn to isolated nucleic acids including SEQ ID Nos: 4, 8, or 15. This argument has been considered and is found persuasive.

Specification

The preliminary amendment filed March 2, 2000 (Paper No. 5) is objected to. The attempt to change "set out at" to --- included in--- was not entered because it appears the section referenced to in the specification (page 12, line 10) was incorrect.

Further, on page 12, line 11, after the word "acids" the specification has been amended to recite "This is set forth as SEQ ID NO:6".. as requested in Paper No. 5. However, a second preliminary amendment filed June 27, 2000 (Paper No. 7) also requested a similar change on page 12, line 11 which inserted the text, "See SEQ ID NO:6". Applicant is requested to cancel one of these recitations to avoid redundancy. All of the other amendments have been properly incorporated into the specification.

Further, the specification on page 11, is objected to. Specifically, the 21 nucleotide sequence for SEQ ID NO:11 appears to be incorrect because the last nucleotide is a listed as "C", but the as filed sequence listing reveals that the last nucleotide of SEQ ID NO:11 is a "T". Clarification and corrections are requested.

Claim Objections

Claim 86 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 87. (This also makes claims 88 and 89, 90 and 91, etc.. duplicates of each other). When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper to object to the claims as being substantial duplicates. See MPEP § 706.03(k).

Claims 81-84 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 80, and 85-96 are indefinite for reciting the phrase "stringent conditions" in Claim 80. Stringent conditions are not defined by the claims, which include the full range of stringent conditions, that is from very permissive to very high stringency. Further, the specification does

not provide a standard for ascertaining the requisite degree of stringent conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 80, and 85-96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth an isolated nucleic acid molecule comprising SEQ ID NO:4, 8, or 15 and or the "complete" complement thereof, and therefore the written description is not commensurate in scope with the claims drawn to naturally occurring polynucleotide sequences and or complementary sequences which hybridize under stringent conditions.

The claims are broadly drawn to an isolated nucleic acid molecule, the complementary sequence of which hybridizes, under stringent conditions, to one of the nucleotide sequences set forth in SEQ ID NO:4, 8, or 15.

Thus, the claims broadly include a whole universe of polynucleotide fragments. Clearly, it would be expected that a substantial number of the hybridizing or complementary polynucleotides encompassed by the claims **would not** share either structural or functional

properties with polynucleotides of SEQ ID NO:4, 8, or 15. Further, the claims do not require that the polynucleotides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a chemical structure in the form of a wide variety of potential hybridizing nucleic acids. Further, there is no identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

With the exception of SEQ ID NOs: 4, 8, or 15, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved

until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Therefore, only an isolated nucleic acid molecule comprising SEQ ID NO:4, 8, or 15 and or the complete complements thereof meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 80, 85-87, and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by GARKAVSTEV *et al.* (WO 97/21809, June 19, 1997).

Garkavstev *et al.* teach an isolated nucleic acid molecule with 70% overall sequence similarity to SEQ ID NO:4 and 35% overall similarity to SEQ ID NO:8 (see attached sequence listings at the end of this Action) each of which would inherently hybridize under stringent conditions to SEQ ID NO:4. Garkavstev *et al.* further teach expression vectors operably linked to

a promoter comprising said nucleic acid molecule (page 19, lines 15-21), recombinant cells transformed or transfected with said isolated nucleic acids (page 5, lines 5+), and viral expression vectors (page 20, lines 20+) which would inherently be characterized as mutated or attenuated.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
May 12, 2003

Gary B. Nickol

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PR   24-OCT-2000; 2000US-0602362.
XX
PA   (LUDW-) LUDWIG INST CANCER RES.
PA   (SLOK ) SLOAN KETTERING INST CANCER RES.
PA   (CORR ) CORNELL RES FOUND INC.
XX
PI   Jager D,  Stockert E,  Scanlan M,  Knuth A,  Old L,  Gure A,  Chen Y;
XX
DR   WPI; 2001-441706/47.
DR   P-PSDB; AAB84698.
XX
PT   Isolated cancer associated nucleic acid molecule identified by SEREX
PT   (serological identification of antigens by recombinant expression
PT   cloning) technique, useful in nucleic acid based therapies to treat
PT   cancer -
XX
PS   Claim 1; Page 43-44; 62pp; English.
XX
CC   The present sequence encodes a human cancer associated antigen.
CC   The sequence is a variant of the ING1 gene, which is a tumour
CC   suppressor gene candidate. The cancer associated antigen polynucleotides
CC   and polypeptides are useful for screening for the possible presence of
CC   a pathological condition in a subject such as cancer. The cancer
CC   associated antigen polypeptides are useful for producing vaccines.
XX
SQ   Sequence 1533 BP; 336 A; 431 C; 521 G; 244 T; 1 other;

  Query Match             35.8%;  Score 276;  DB 22;  Length 1533;
  Best Local Similarity   80.8%;  Pred. No. 1.9e-64;
  Matches  422;  Conservative    0;  Mismatches   60;  Indels   40;  Gaps    7;

Qy       2 AAGCGTTCTCGGCGGCAGCGCAACAACTAGAACCGTGAGAACGCGTCCAGCAACCGCGAC 61
Db     892 AAGCGCTCACGGCGGCAGCGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGA- 950

Qy      62 CCACGACGACGTCACCTCGGGCACGCCCAAGGAGAAGAAAGCCCAGACCTCTAAGAAGAA 121
Db     951 CCACGACGACGGCGCCTCGGGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAA 1010

Qy     122 GCAGGGCTCCATGGCCAAGGCGTAGCGGCAGGCGTCCCCCGCAGACCTCCCCATCGACCC 181
Db    1011 GAAGCGCTCCAAGGCCAAGGCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCC 1070

Qy     182 CAGCGAGCC----------------------CTCCTACTGGGAGATGATCCGCTGCGA 217
Db    1071 CAACGAACCCACGTACTGTCTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGA 1130

Qy     218 CA---ACGAATGCCCCATCGAGTGGTTCCGCTTCTCGTGTGTGAGTCTCAACCATAAACC 274
Db    1131 CAACGACGAGTGCCCCATCGAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACC 1190

Qy     275 AAAGCGCAAGTGGTACTGTTCCAGATGCCGGGGAAAGAACG--------ATGGGCAAAGC 326
Db    1191 CAAGGGCAAGTGGTACTGTCCCAAGTGCCGGGGGGAGAACGAGAAGACCATGGACAAAGC 1250

Qy     327 CCTTGAGAAGTCCAGAAAAAAAACAGGGCTTATAACAGGTAGTTTGGGGACATGCGTCTA 386
Db    1251 CCTGGAGAAATCCA--AAAAAGAGAGGGCTTACAACAGGTAGTTTGTGGACAGGCGCCTG 1308

Qy     387 ATAGTGAGGAGAACAAAATAAGCCAGTGTGTTGATTACATTGCCACCTTTGCTGAGGTGC 446
Db    1309 GT-GTGAGGAGGACAAAATAAACC-GTGTATTTATTACATTGCTGCCTTTGTTGAGGTGC 1366

Qy     447 AGGAAGTGTAAAATGTATATTTTTAAAGAATGTTGTTACAGG 488
Db    1367 AAGGAGTGTAAAATGTATATTTTTAAAGAATGTTAGAAAAGG 1408


RESULT 5
AAT69651
ID   AAT69651 standard; cDNA; 1902 BP.
XX
AC   AAT69651;
XX
DT   27-AUG-1997  (first entry)
XX
DE   Tumour suppressor gene ING1 partial cDNA.
XX
KW   Tumour suppressor gene; ING1; p33ING1; breast cancer; brain cancer;
KW   diagnosis; gene therapy; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             109..741
FT                   /*tag= a
XX
PN   WO9721809-A1.
XX
PD   19-JUN-1997.
XX
PF   06-DEC-1996;   96WO-CA00819.
XX
PR   15-NOV-1996;   96US-0751230.
PR   08-DEC-1995;   95US-0569721.
XX
PA   (UYTE-) UNIV TECHNOLOGIES INT INC.
XX
PI   Garkavstev I,  Riabowol K;
XX
DR   WPI; 1997-332781/30.
DR   P-PSDB; AAW19118.
XX
PT   Isolated tumour suppressor gene, ING1 - useful to develop products
PT   for inhibiting or increasing cell proliferation, in particular for
PT   treatment or diagnosis of cancer
XX
PS   Claim 1; Fig 2; 63pp; English.
XX
CC   A partial cDNA clone (AAT69651), designated ING1, codes for a novel
CC   tumour suppressor protein p33ING1 (AAW19118) that is a potent
CC   inhibitor of cell growth.  It was isolated by subtractive
CC   hybridisation between normal mammary and transformed epithelial
CC   cDNAs, isolation of an antisense ING1 cDNA insert that caused
CC   increased cell proliferation, and use of the insert to screen
CC   normal human fibroblast and HeLa cDNA libraries.  A complete ING1
CC   sequence (AAT69652) was obtd. by 5'RACE.  ING1 is localised to the
CC   13q33-34 chromosome region, to which a number of human cancers have
CC   been mapped.  ING1 nucleic acids can be used in the diagnosis of
CC   breast cancer; a decreased level of ING1 mRNA indicates cancerous
CC   cells.  They can also be used in gene therapy methods to block the
CC   proliferation of cancer cells.
XX
SQ   Sequence 1902 BP; 574 A; 391 C; 461 G; 476 T; 0 other;

  Query Match             35.8%;  Score 276;  DB 18;  Length 1902;
  Best Local Similarity   80.8%;  Pred. No. 2e-64;
  Matches  422;  Conservative    0;  Mismatches   60;  Indels   40;  Gaps    7;

Qy       2 AAGCGTTCTCGGCGGCAGCGCAACAACTAGAACCGTGAGAACGCGTCCAGCAACCGCGAC 61
Db     343 AAGCGCTCACGGCGGCAGCGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGA- 401

Qy      62 CCACGACGACGTCACCTCGGGCACGCCCAAGGAGAAGAAAGCCCAGACCTCTAAGAAGAA 121
Db     402 CCACGACGACGGCGCCTCGGGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAA 461

Qy     122 GCAGGGCTCCATGGCCAAGGCGTAGCGGCAGGCGTCCCCCGCAGACCTCCCCATCGACCC 181
Db     462 GAAGCGCTCCAAGGCCAAGGCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCC 521

Qy     182 CAGCGAGCC----------------------CTCCTACTGGGAGATGATCCGCTGCGA 217
Db     522 CAACGAACCCACGTACTGTCTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGA 581

Qy     218 CA---ACGAATGCCCCATCGAGTGGTTCCGCTTCTCGTGTGTGAGTCTCAACCATAAACC 274
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```
Db    582 CAACGACGAGTGCCCCATCGAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACC 641

Qy    275 AAAGCGCAAGTGGTACTGTTCCAGATGCCGGGGAAAGAACG--------ATGGGCAAAGC 326

Db    642 CAAGGGCAAGTGGTACTGTCCCAAGTGCCGGGGGGAGAACGAGAAGACCATGGACAAAGC 701

Qy    327 CCTTGAGAAGTCCAGAAAAAAAAACAGGGCTTATAACAGGTAGTTTGGGGACATGCGTCTA 386

Db    702 CCTGGAGAAATCCA--AAAAAGAGAGGGCTTACAACAGGTAGTTTGTGGACAGGCGCCTG 759

Qy    387 ATAGTGAGGAGAACAAAATAAGCCAGTGTGTTGATTACATTGCCACCTTTGCTGAGGTGC 446

Db    760 GT-GTGAGGAGGACAAAATAAACC-GTGTATTTATTACATTGCTGCCTTTGTTGAGGTGC 817

Qy    447 AGGAAGTGTAAAATGTATATTTTTAAAGAATGTTGTTAGAGG 488

Db    818 AAGGAGTGTAAAATGTATATTTTTAAAGAATGTTAGAAAAGG 859
```

RESULT 6
62285
AAV62285 standard; cDNA; 1902 BP.
XX
AC AAV62285;
XX
DT 18-JAN-1999 (first entry)
XX
DE Partial ING1 partial cDNA sequence.
XX
KW ING1 gene; p33ING1; human; apoptosis; cell death; breast cancer;
KW brain tumour; gene therapy; tumour suppressor; ss.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT CDS 109..741
FT /*tag= a
XX
PN WO9844102-A2.
XX
PD 08-OCT-1998.
XX
PF 26-MAR-1998; 98WO-CA00277.
XX
PR 27-MAR-1997; 97US-0828158.
XX
PA (UYTE-) UNIV TECHNOLOGIES INT INC.
XX
Garkavtsev I, Helbing CC, Johnston RN, Riabowol K;

WPI; 1998-542700/46.
DR P-PSDB; AAW79674.
XX
PT Modulating eukaryotic apoptosis by increasing p33ING1 activity -
PT- using p33ING1 derivatives, to induce apoptosis in cancer cells, and
PT in the investigation of apoptotic pathways
XX
PS Example 2; Fig 2; 66pp; English.
XX
CC This is the nucleotide sequence of a human ING1 (INhibitor of
CC Growth) partial cDNA clone that codes for a p33ING1 polypeptide
CC (see AAW79674), a novel inhibitor of cell growth and a candidate
CC tumour suppressor. ING1 is a new gene that is expressed in normal
CC mammary epithelial cells, but which is expressed only at lower
CC levels in several cancerous mammary epithelial cell lines and is
CC not expressed in many primary brain tumours. To isolate ING1, a
CC subtractive hybridisation of breast cancer cell line cDNAs was
CC performed with cDNA from normal mammary epithelial cells, and
CC subtracted cDNAs were cloned into retrovirus vector pLNCX.
CC Following passage through a packaging line, normal mouse mammary
CC epithelial cells were infected, and infected cells were injected
CC into mice. Putative transforming fragments from tumours were
CC isolated by PCR (see AAV62290-91) and subcloned into LNCX. An ING1
CC fragment was obtained and used to screen normal human fibroblast
CC and HeLa cell cDNA libraries. 2 Clones were sequenced to obtain
CC the partial ING1 sequence. The complete cDNA sequence (see
CC AAV62292) was obtained by RACE. A claimed method to potentiate
CC apoptosis in a eukaryotic cell involves administering an active
CC p33ING1 peptide or an oligonucleotide encoding such as a peptide.
CC A claimed method for inhibiting apoptosis in a eukaryotic cell
CC involves administering an antisense oligonucleotide. Also claimed
CC are a method for determining the apoptotic characteristics of a
CC eukaryotic cell, an assay for determining the level of p33ING1
CC activity in a eukaryotic cell, and an isolated eukaryotic cell
CC substantially free of p33ING1 biological activity. The invention
CC discloses ING1 derivatives or variants that may be used to induce
CC apoptosis in eukaryotic cancer cells.
XX
SQ Sequence 1902 BP; 574 A; 390 C; 462 G; 476 T; 0 other;

Query Match 35.8%; Score 276; DB 19; Length 1902;
Best Local Similarity 80.8%; Pred. No. 2e-64;
Matches 422; Conservative 0; Mismatches 60; Indels 40; Gaps 7;

```
Qy      2 AAGCGTTCTCGGCGGCAGCGCAACAACTAGAACCGTGAGAACGCGTCCAGCAACCGCGAC 61

Db    343 AAGCGCTCACGGCGGCAGCGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGA- 401

Qy     62 CCACGACGACGTCACCTCGGGCACGCCCAAGGAGAAGAAAGCCCAGACCTCTAAGAAGAA 121

Db    402 CCACGACGACGGCGCCTCGGGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAA 461

Qy    122 GCAGGGCTCCATGGCCAAGGCGTAGCGGCAGGCGTCCCCCGCAGACCTCCCCATCGACCC 181

Db    462 GAAGCGCTCCAAGGCCAAGGCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCC 521

Qy    182 CAGCGAGCC----------------------CTCCTACTGGGAGATGATCCGCTGCGA 217

Db    522 CAACGAACCCACGTACTGTCTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGA 581

Qy    218 CA---ACGAATGCCCCATCGAGTGGTTCCGCTTCTCGTGTGTGAGTCTCAACCATAAACC 274

Db    582 CAACGACGAGTGCCCCATCGAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACC 641

Qy    275 AAAGCGCAAGTGGTACTGTTCCAGATGCCGGGGAAAGAACG--------ATGGGCAAAGC 326

Db    642 CAAGGGCAAGTGGTACTGTCCCAAGTGCCGGGGGGAGAACGAGAAGACCATGGACAAAGC 701

Qy    327 CCTTGAGAAGTCCAGAAAAAAAAACAGGGCTTATAACAGGTAGTTTGGGGACATGCGTCTA 386

Db    702 CCTGGAGAAATCCA--AAAAAGAGAGGGCTTACAACAGGTAGTTTGTGGACAGGCGCCTG 759

Qy    387 ATAGTGAGGAGAACAAAATAAGCCAGTGTGTTGATTACATTGCCACCTTTGCTGAGGTGC 446

Db    760 GT-GTGAGGAGGACAAAATAAACC-GTGTATTTATTACATTGCTGCCTTTGTTGAGGTGC 817

Qy    447 AGGAAGTGTAAAATGTATATTTTTAAAGAATGTTGTTAGAGG 488

Db    818 AAGGAGTGTAAAATGTATATTTTTAAAGAATGTTAGAAAAGG 859
```

RESULT 7
AAT69652
ID AAT69652 standard; cDNA; 2061 BP.
XX
AC AAT69652;
XX
DT 27-AUG-1997 (first entry)
XX
DE Tumour suppressor gene ING1 full-length cDNA.
XX
KW Tumour suppressor gene; ING1; p33ING1; breast cancer; brain cancer;
KW diagnosis; gene therapy; ss.
XX
OS Homo sapiens.

```
Qy    542 AACAGCAAGCGCTCACGGCGGCAGCGCAACAACGAGAACCGTGAGAACGCGTCCAGCAAC 601
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    480 AACAGCAAGCGCTCACGGCGGCAGCGCAACAACGAGAACCGTGAGAACGCGTCCAGCAAC 539

Qy    602 CACGACCACGACGACGGCGCCTCGGGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAG 661
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    540 CACGACCACGACGACGGCGCCTCGGGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAG 599

Qy    662 AAGAAGAAGCGCTCCAAGGCCAAGGCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATC 721
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    600 AAGAAGAAGCGCTCCAAGGCCAAGGCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATC 659

Qy    722 GACCCCAACGAACCCACGTACTGTCTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGC 781
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    660 GACCCCAACGAACCCACGTACTGTCTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGC 719

Qy    782 TGCGACAACGACGAGTGCCCCATCGAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCAT 841
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    720 TGCGACAACGACGAGTGCCCCATCGAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCAT 779

Qy    842 AAACCCAAGGGCAAGT 857
          ||||||||||||||||
Db    780 AAACCCAAGGGCAAGT 795
```

RESULT 8
AAH28479
ID AAH28479 standard; DNA; 1143 BP.
XX
AC AAH28479;
XX
DT 17-SEP-2001 (first entry)
XX
DE Nucleotide sequence of a human cancer associated antigen.
XX
KW Cancer associated antigen; ING1; tumour suppressor; cancer; vaccine; ss.
XX
OS Homo sapiens.
XX
FH Key   Location/Qualifiers
FT CDS   16..900
FT   /*tag= a
FT   /transl_except= "(pos: 25..30, aa: Cys)"
FT   /transl_except= "(pos: 124..126, aa: Pro, Ala)"
FT   /poroduct= "cancer asscociated antigen"
XX
PN WO200147959-A2.
XX
PD 05-JUL-2001.
XX
PF 29-NOV-2000; 2000WO-US42334.
XX
PR 30-NOV-1999; 99US-0451739.
PR 24-OCT-2000; 2000US-0602362.
XX
PA (LUDW-) LUDWIG INST CANCER RES.
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PA (CORR) CORNELL RES FOUND INC.
XX
PI Jager D, Stockert E, Scanlan M, Knuth A, Old L, Gure A, Chen Y;
XX
DR WPI; 2001-441706/47.
DR P-PSDB; AAB84697.
XX
PT Isolated cancer associated nucleic acid molecule identified by SEREX
PT (serological identification of antigens by recombinant expression
PT cloning) technique, useful in nucleic acid based therapies to treat
PT cancer -
XX
PS Example 4; Page 44; 62pp; English.
XX
CC The present sequence encodes a human cancer associated antigen.
CC sequence is the wildtype of the ING1 gene, which is a tumour
CC suppressor gene candidate. The cancer associated antigen polynucleotides
CC and polypeptides are useful for screening for the possible presence of
CC a pathological condition in a subject such as cancer. The cancer
CC associated antigen polypeptides are useful for producing vaccines.
XX
SQ Sequence 1143 BP; 289 A; 291 C; 366 G; 197 T; 0 other;

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  Query Match             70.7%;  Score 605.6;  DB 22;  Length 1143;
  Best Local Similarity   95.6%;  Pred. No. 3.7e-109;
  Matches  623;  Conservative    0;  Mismatches   29;  Indels    0;  Gaps    0;

Qy    206 CTAGGCTGCTGGGAGTGGTGGTCCGGCCGCGGAATGGAGATCCTGAAGGAGCTAGACGAG 265
          ||  | |  ||  | |  | |  | |  | |  | |  ||||||||||||||||||||||||
Db    160 CTGACCCGAGGGTGGGGCCGCGCGTGGCCGTGGAAACAGATCCTGAAGGAGCTAGACGAG 219

Qy    266 TGCTACGAGCGCTTCAGTCGCGAGACAGACGGGGCGCAGAAGCGGCGGATGCTGCACTGT 325
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    220 TGCTACGAGCGCTTCAGTCGCGAGACAGACGGGGCGCAGAAGCGGCGGATGCTGCACTGT 279

Qy    326 GTGCAGCGCGCGCTGATCCGCAGCCAGGAGCTGGGCGACGAGAAGATCCAGATCGTGAGC 385
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    280 GTGCAGCGCGCGCTGATCCGCAGCCAGGAGCTGGGCGACGAGAAGATCCAGATCGTGAGC 339

Qy    386 CAGATGGTGGAGCTGGTGGAGAACCGCACGCGGCAGGTGGACAGCCACGTGGAGCTGTTC 445
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    340 CAGATGGTGGAGCTGGTGGAGAACCGCACGCGGCAGGTGGACAGCCACGTGGAGCTGTTC 399

Qy    446 GAGGCGCAGCAGGAGCTGGGCGACACAGCGGGCAACAGCGGCAAGGCTGGCGCGGACAGG 505
          |||||||||||||||||||||||||||||| |||||||||||||||| ||||||||||||
Db    400 GAGGCGCAGCAGGAGCTGGGCGACACAGTGGGCAACAGCGGCAAGGTTGGCGCGGACAGG 459

Qy    506 CCCAAAGGCGAGGCGGCAGCGCAGGCTGACAAGCCCAACAGCAAGCGCTCACGGCGGCAG 565
          ||||| ||||| |||| ||||||| ||||||||||||||||||||||||||||||||||||
Db    460 CCCAATGGCGATGCGGTAGCGCAGTCTGACAAGCCCAACAGCAAGCGCTCACGGCGGCAG 519

Qy    566 CGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGACCACGACGACGGCGCCTCG 625
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    520 CGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGACCACGACGACGGCGCCTCG 579

Qy    626 GGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAAGAAGCGCTCCAAGGCCAAG 685
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    580 GGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAAGAAGCGCTCCAAGGCCAAG 639

Qy    686 GCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCCCAACGAACCCACGTACTGT 745
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    640 GCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCCCAACGAACCCACGTACTGT 699

Qy    746 CTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGACAACGACGAGTGCCCCATC 805
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    700 CTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGACAACGACGAGTGCCCCATC 759

Qy    806 GAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACCCAAGGGCAAGT 857
          ||||||||||||||||||||||||||||||||||||||||||||||||||
Db    760 GAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACCCAAGGGCAAGT 811
```

RESULT 9
AAT69651
ID AAT69651 standard; cDNA; 1902 BP.
XX
AC AAT69651;
XX
DT 27-AUG-1997 (first entry)
XX
DE Tumour suppressor gene ING1 partial cDNA.
XX
KW Tumour suppressor gene; ING1; p33ING1; breast cancer; brain cancer;
KW diagnosis; gene therapy; ss.
XX
OS Homo sapiens.
XX
FH Key   Location/Qualifiers
FT CDS   109..741

```
FT                   /*tag=  a
XX
PN   WO9721809-A1.
XX
PD   19-JUN-1997.
XX
PF   06-DEC-1996;   96WO-CA00819.
XX
PR   15-NOV-1996;   96US-0751230.
PR   08-DEC-1995;   95US-0569721.
XX
PA   (UYTE-) UNIV TECHNOLOGIES INT INC.
XX
PI   Garkavstev I,  Riabowol K;
XX
DR   WPI; 1997-332781/30.
DR   P-PSDB; AAW19118.
XX
PT   Isolated tumour suppressor gene, ING1 - useful to develop products
PT   for inhibiting or increasing cell proliferation, in particular for
PT   treatment or diagnosis of cancer
XX
PS   Claim 1; Fig 2; 63pp; English.
XX
CC   A partial cDNA clone (AAT69651), designated ING1, codes for a novel
CC   tumour suppressor protein p33ING1 (AAW19118) that is a potent
CC   inhibitor of cell growth.  It was isolated by subtractive
CC   hybridisation between normal mammary and transformed epithelial
CC   cDNAs, isolation of an antisense ING1 cDNA insert that caused
CC   increased cell proliferation, and use of the insert to screen
CC   normal human fibroblast and HeLa cDNA libraries.  A complete ING1
CC   sequence (AAT69652) was obtd. by 5'RACE.  ING1 is localised to the
CC   13q33-34 chromosome region, to which a number of human cancers have
CC   been mapped.  ING1 nucleic acids can be used in the diagnosis of
CC   breast cancer; a decreased level of ING1 mRNA indicates cancerous
CC   cells.  They can also be used in gene therapy methods to block the
CC   proliferation of cancer cells.
XX
SQ   Sequence 1902 BP; 574 A; 391 C; 461 G; 476 T; 0 other;

  Query Match          70.7%;  Score 605.6;  DB 18;  Length 1902;
  Best Local Similarity  95.6%;  Pred. No. 3.8e-109;
  Matches  623;  Conservative    0;  Mismatches   29;  Indels    0;  Gaps    0;

Qy    206 CTAGGCTGCTGGGAGTGGTGGTCCGGCCGCGGAATGGAGATCCTGAAGGAGCTAGACGAG 265
          ||   | |  ||  | |  | |  | |  | |  ||||||||||||||||||||||
Db      1 CTGACCCGAGGGTGGGGCCGCGCGTGGCCGTGGAAACAGATCCTGAAGGAGCTAGACGAG 60

Qy    266 TGCTACGAGCGCTTCAGTCGCGAGACAGACGGGGCGCAGAAGCGGCGGATGCTGCACTGT 325
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TGCTACGAGCGCTTCAGTCGCGAGACAGACGGGGCGCAGAAGCGGCGGATGCTGCACTGT 120

Qy    326 GTGCAGCGCGCGCTGATCCGCAGCCAGGAGCTGGGCGACGAGAAGATCCAGATCGTGAGC 385
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 GTGCAGCGCGCGCTGATCCGCAGCCAGGAGCTGGGCGACGAGAAGATCCAGATCGTGAGC 180

Qy    386 CAGATGGTGGAGCTGGTGGAGAACCGCACGCGGCAGGTGGACAGCCACGTGGAGCTGTTC 445
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 CAGATGGTGGAGCTGGTGGAGAACCGCACGCGGCAGGTGGACAGCCACGTGGAGCTGTTC 240

Qy    446 GAGGCGCAGCAGGAGCTGGGCGACACAGCGGGCAACAGCGGCAAGGCTGGCGCGGACAGG 505
          |||||||||||||||||||||||| |||||||||||||||| ||||||||||||||||||
Db    241 GAGGCGCAGCAGGAGCTGGGCGACACAGTGGGCAACAGCGGCAAGGTTGGCGCGGACAGG 300

Qy    506 CCCAAAGGCGAGGCGGCAGCGCAGGCTGACAAGCCCAACAGCAAGCGCTCACGGCGGCAG 565
          ||||| |||||  |||| ||||||| ||||||||||||||||||||||||||||||||||
Db    301 CCCAATGGCGATGCGGTAGCGCAGTCTGACAAGCCCAACAGCAAGCGCTCACGGCGGCAG 360

Qy    566 CGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGACCACGACGACGGCGCCTCG 625
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 CGCAACAACGAGAACCGTGAGAACGCGTCCAGCAACCACGACCACGACGACGGCGCCTCG 420

Qy    626 GGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAAGAAGCGCTCCAAGGCCAAG 685
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 GGCACACCCAAGGAGAAGAAGGCCAAGACCTCCAAGAAGAAGAAGCGCTCCAAGGCCAAG 480

Qy    686 GCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCCCAACGAACCCACGTACTGT 745
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 GCGGAGCGAGAGGCGTCCCCTGCCGACCTCCCCATCGACCCCAACGAACCCACGTACTGT 540

Qy    746 CTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGACAACGACGAGTGCCCCATC 805
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 CTGTGCAACCAGGTCTCCTATGGGGAGATGATCGGCTGCGACAACGACGAGTGCCCCATC 600

Qy    806 GAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACCCAAGGGCAAGT 857
          |||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 GAGTGGTTCCACTTCTCGTGCGTGGGGCTCAATCATAAACCCAAGGGCAAGT 652


RESULT 10
AAV62285
ID   AAV62285 standard; cDNA; 1902 BP.
XX
AC   AAV62285;
XX
DT   18-JAN-1999  (first entry)
XX
DE   Partial ING1 partial cDNA sequence.
XX
KW   ING1 gene; p33ING1; human; apoptosis; cell death; breast cancer;
KW   brain tumour; gene therapy; tumour suppressor; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             109..741
FT                   /*tag=  a
XX
PN   WO9844102-A2.
XX
PD   08-OCT-1998.
XX
PF   26-MAR-1998;   98WO-CA00277.
XX
PR   27-MAR-1997;   97US-0828158.
XX
PA   (UYTE-) UNIV TECHNOLOGIES INT INC.
XX
PI   Garkavtsev I,  Helbing CC,  Johnston RN,  Riabowol K;
XX
DR   WPI; 1998-542700/46.
DR   P-PSDB; AAW79674.
XX
PT   Modulating eukaryotic apoptosis by increasing p33ING1 activity -
PT   using p33ING1 derivatives, to induce apoptosis in cancer cells, and
PT   in the investigation of apoptotic pathways
XX
PS   Example 2; Fig 2; 66pp; English.
XX
CC   This is the nucleotide sequence of a human ING1 (INhibitor of
CC   Growth) partial cDNA clone that codes for a p133ING1 polypeptide
CC   (see AAW79674), a novel inhibitor of cell growth and a candidate
CC   tumour suppressor.  ING1 is a new gene that is expressed in normal
CC   mammary epithelial cells, but which is expressed only at lower
CC   levels in several cancerous mammary epithelial cell lines and is
CC   not expressed in many primary brain tumours.  To isolate ING1, a
CC   subtractive hybridisation of breast cancer cell line cDNAs was
CC   performed with cDNA from normal mammary epithelial cells, and
CC   subtracted cDNAs were cloned into retrovirus vector pLNCX.
CC   Following passage through a packaging line, normal mouse mammary
CC   epithelial cells were infected, and infected cells were injected
CC   into nude mice.  Putative transforming fragments from tumours were
CC   isolated by PCR (see AAV62290-91) and subcloned into LNCX.  An ING1
CC   fragment was obtained and used to screen normal human fibroblast
CC   and HeLa cell cDNA libraries.  2 Clones were sequenced to obtain
CC   the partial ING1 sequence.  The complete cDNA sequence (see
```